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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/816,755	03/23/2001	Nagarajan Vaidehi	06618-606001/CIT3191	4783

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EXAMINER	
MILLER, MARINA I	
ART UNIT	PAPER NUMBER
1631	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/816,755	VAIDEHI ET AL.	
	Examiner	Art Unit	
	Marina Miller	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,35-57 and 59-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 35-57, and 59-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' submission filed on 11/2/2006 is acknowledged.

Claims 1, 3, 35-57, and 59-64 are pending.

Claims 2, 4-34, and 58 are cancelled.

Claims 1, 3, 35-57, and 59-64 presently are under examination.

Applicants' arguments have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are applied.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101

Claims 1, 3, and 35-57, 59-60, and 64 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1, 3, and 35-57, and 59-60 were previously rejected for reciting non-statutory subject matter because the claimed method neither transforms or reduces an article or a physical object to a different stage or thing nor recites tangible expression of optimizing the full-atom model in a form useful to one skilled in the art.

Applicants argue that "it is not the outputting a result of a calculation in a particular form that is a pre-requisite for finding a claimed process statutory, but instead it is the ability of others to access the result."

In response, it is noted that "the ability of others to access a result" means that the result is "provided" or "outputted" to others. The outputting or providing a result does not necessarily mean "sending to a printer" (see the applicants' answer, page 15, second full paragraph); it only means that the result is saved in a particular format/location accessible to a user or communicated to a user in some form (*e.g.*, via the Internet). The instant method does not recite any providing or outputting the result to a user, and therefore others do not have the ability to access the result. Thus, the method does not recite steps of producing something that is concrete, useful, and tangible, and is not statutory.

It is noted that claim 61 recites outputting the predicted structure in protein data bank format (*i.e.*, in a format that can be interpreted/used by a user), and therefore is statutory.

For the reasons stated above and in the previous office action, the examiner maintains the rejection of claims 1, 3, and 35-57, and 59-60.

New claim 64 depends from claims 1 and 45, and is rejected for the same reasons set forth above.

Claim Rejections - 35 USC § 112

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 35-57, and 59-64 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claim 1, as amended, is directed to a method comprising steps of "assembling ... helices into a helix bundle" and "optimizing configuration of the helix bundle." However, optimizing configuration of a helical bundle, *per se*, does not have support in the specification, claims, or drawings, as originally filed. Applicants point to support in paragraph [0016] of the originally filed specification. The specification in paragraph [0016] discloses combining helices to form a helix bundle, *assembling the helix bundle with a lipid bilayer to form a system helix bundle*, and optimizing the structure of the *system* helix bundle. The originally filed claims recite "optimizing a helix bundle configuration" which is not equivalent to "optimizing configuration of the helix bundle." "A helix bundle configuration" is interpreted in light of the disclosure to be a helical bundle modeled in a lipid bilayer (*i.e.*, in a membrane with solvent). The specification does not disclose optimizing a configuration of a helix bundle, *per se*, but only in a membrane with solvent. For these reasons, the claims are rejected for reciting new matter.

Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement

and whether any necessary experimentations is "undue." These factors include, but are not limited to:

a) The breadth of the claims;
b) The nature of the invention;
c) The state of the prior art;
d) The level of one of ordinary skill;
e) The level of predictability in the art;
f) The amount of direction provided by the inventor;
g) The existing of working examples; and
h) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. 858 F.2d at 740. While all of these factors are considered, sufficient amount for a prima facie case are discussed below.

Claims 1, 3, 35-57, and 59-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for providing a structure of G-protein coupled receptors, does not reasonably provide enablement for ALL membrane spanning proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

a) The claims are broad because they are drawn to a generic method for predicting structure of a membrane-bound protein having a plurality of helical regions. While the specification discloses how to predict structure of G-protein coupled receptors, it fails to guide one skilled in the art how to predict a structure of any membrane-spanning protein without knowing how helices interact with a membrane and each other, how they fit into a bundle; i.e.without knowing anything about protein tertiary and quaternary structure of the protein to be

modeled. Without knowing any specific information with regard to the arrangement of helices within a membrane, predicting protein structure would require undue experimentation.

b) The invention is drawn to a method for predicting structure of a membrane-spanning protein.

c, e) The prior art analysis shows that modeling proteins is very complicated and has a high degree of uncertainty. For example, as late as 2005, Ginalski disclosed that "[t]heoretically, it should be possible to deduce structure from sequence by accurate simulation of physical processes. We are very far from achieving this goal, and the methods of practical importance were traditionally based on the observation that proteins with similar sequences are structurally similar as well." Ginalski, *NAR*, 33(6):1874-1891 (2005). Ginalski also discloses that "despite recent efforts to develop automated protein structure determination protocols, structural genomics projects are slow in generating fold assignments for complete proteomics, and spatial structures remain unknown for many protein families." *Id.* at 1874. *See also* Standley, *Proteins: Structure, Function, and Genetics*, 33:240-252 (1998); and Saven, *JMB*, 257:199-216 (1996), showing that predicting a protein structure of an protein with a previously unknown structure is not a trivial task. Thus, the prior art discloses that although folding of one protein (or a family of proteins) is known, other proteins, specifically proteins not in that family, are NOT necessarily expected to be assembled the same way.

d) The skill of those in the art of molecular modeling and bioinformatics is high.

f) The specification does not provide guidance for predicting protein structure of any membrane-spanning proteins other than those which are G-protein coupled receptors.

g) The specification provides working examples only for G-protein coupled receptors, for which the crystal structures have been fitted in the transmembrane region of the protein. The specification does not provide working example of any other protein or protein family, and also does not teach how to predict a structure of all transmembrane proteins based on the structure predicted for G-protein coupled receptors.

h) In order to practice the claimed invention, one skilled in the art must randomly select parameters for "fitting" helices and must guess what parameters to use for structure optimization. This constitutes undue experimentation.

Due to the undue experimentation required to obtain the goal of the invention, the lack of directions presented in the specification, the complex nature of the invention, and the state of the prior art showing a high degree of uncertainty in modeling proteins, the specification fails to teach one skilled in the art how to use the claimed method for predicting protein structure of transmembrane proteins.

Second Paragraph

Claims 1, 3, 35-57, and 59-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, as amended, recites the limitation "to provide a predicted structure." It is not clear whether "providing" is intended to be an active, positive method step or merely an intended result of the method. As the intended limitation is unclear, the claim is indefinite. Claims 3, 35-

37, and 59-64 are also indefinite as they depend from claim 1 and do not correct the indefiniteness thereof

Conclusion

No claims are allowed.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-6, M-Thu.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, Ph. D. can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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11/22/07